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Correlation of CD44, VEGF-C and COX-2 with clinicopathologic parameters and clinical outcomes

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Background: Recent studies suggest that CD44-ligation induces expression of vascular endothelial growth factor-C (VEGF-C) expression and that the induction of the cyclooxygenase (COX-2) is achieved through an upregulation of VEGF-C. It is postulated that individual role of CD44, VEGF-C and COX-2 involves cellular proliferation, angiogenesis and metastasis of cancer. We investigated the correlation of CD44, VEGF-C and COX-2 with clinicopathologic parameters and clinical outcomes in surgically resected NSCLC patients.

Methods: Using immunohistochemial staining, we analyzed the protein expressions of CD44s, CD44v6, COX-2 and VEGF-C on the tissue array specimens from 180 patients (adenocarcinoma (AC), n=90; squamous cell carcinoma (SCC), n=90) with completely resected NSCLC patients.

Results: The median age was 64 (range, 19-88) and M:F ratio was 141:39. According to pathologic stage by AJCC, stage I, II, III was 101 (56.1%), 35 (19.4%) and 44 (24.4%). The expressions of CD44s, CD44v6, COX-2 and VEGF-C were observed in 65.7%, 37.6%, 40% and 60%, respectively. COX-2 overexpression was found in 51.1% of AC subtype and 28.9 % of SCC with statistically significant difference. The expressions of both CD44s and CD44v6 were found to be more frequent in SCC with significance, compared to those of AC (44.6% vs. 26.2%, p<0.001; 6.6% vs. 34.1%, p<0.001). Overexpression of VEGF-C was correlated with CD44 and COX-2 expression. It also had strong correlation with tumor size and differentiation (p=0.026, p=0.004). In the multivariate analysis, only lymph node metastasis was an independent prognostic factor (HR 2.367, p<0.001), but none of these molecules showed statistical correlations.

Conclusions: To be taken, the present study revealed that VEGF-C, correlated with CD44 and COX-2, was a strong predictive marker for tumor size in early stage of NSCLC.

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Risk factors for recurrence and unfavorable prognosis in patients with stage IA non-small-cell lung cancer and a tumor diameter of 20mm or less

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Objective: The purpose of this study was to identify risk factors for disease recurrence and unfavorable prognosis after surgical resection for stage IA non-small-cell lung cancer (NSCLC) in patients with tumor diameters of 20mm or less.

Materials and Methods: One hundred sixty-three patients who had pathologic stage IA NSCLC with tumor diameters ≤ 20mm and who had undergone a lobectomy with mediastinal lymph node dissection were retrospectively reviewed. The relationships between clinicopathological factors and clinical outcomes, including recurrence and survival, were then examined. The clinicopathological factors examined in this study were age, sex, smoking status, preoperative serum carcinoembryonic antigen level, pathologic tumor size, histologic subtype, histologic grade, and visceral pleural invasion.

Results: Among the clinicopathological factors that were examined, the histologic grade of the carcinoma status was significantly related to a high risk of recurrence when analyzed using univariate (P=0.01) and multivariate analyses (P=0.049). Regarding survival, patients with poorly differentiated carcinomas showed a significantly unfavorable overall survival (OS) (P<0.001), disease-specific survival (P=0.003), and disease-free survival (DFS) (P=0.002), compared with patients with well/moderately differentiated carcinomas, according to univariate analyses (Figure). A Cox proportional hazards model indicated that a poorly differentiated carcinoma status was the only independent factor for an unfavorable OS (P=0.02), disease-specific survival (P=0.046) and DFS (P=0.04) (Table).

Conclusion: A lower histologic grade was the only risk factor for recurrence and an unfavorable prognosis for stage IA NSCLC patients with tumor diameters of 20mm or less.

Multivariate analysis for survival

A. Overall survival.

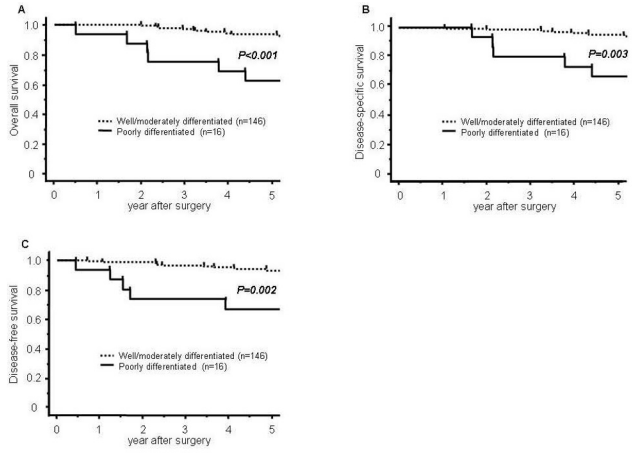
Variables	Hazard ratio	95% C.I.	*P*-value
Age	3.57	0.078-1.01	0.051
Sex	1.27	0.14-11.60	0.83
Smoking status	2.18	0.23-20.64	0.50
Serum CEA level	1.03	0.34-3.08	0.97
Pathologic tumor size	1.67	0.68-4.12	0.26
Histologic subtype	1.06	0.39-2.91	0.90
Histologic grade	3.61	1.24-10.51	0.02
Visceral pleural invasion	4.15	0.49-35.35	0.19

B. Disease-specific survival

Variables	Hazard ratio	95% C.I.	*P*-value
Age	1.71	0.17-2.06	0.40
Sex	2.65	0.063-2.27	0.29
Smoking status	4.20	0.59-30.01	0.15
Serum CEA level	1.23	0.27-5.55	0.79
Pathologic tumor size	1.12	0.35-3.54	0.85
Histologic subtype	0.33	0.040-2.75	0.31
Histologic grade	4.20	1.03-17.12	0.046
Visceral pleural invasion	3.91	0.44-34.83	0.22

C. Disease-free survival

Variables	Hazard ratio	95% C.I.	*P*-value
Age	1.74	0.16-2.02	0.39
Sex	2.51	0.067-2.37	0.31
Smoking status	4.12	0.58-29.31	0.16
Serum CEA level	1.15	0.25-5.25	0.85
Pathologic tumor size	0.98	0.32-3.04	0.98
Histologic subtype	0.36	0.043-2.94	0.34
Histologic grade	4.45	1.09-18.19	0.04
Visceral pleural invasion	5.20	0.58-46.49	0.14



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Survival in lung cancer patients with pathologic fracture

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Background: About 30-40% of all lung cancer patients will develop bone metastases during the course of their disease and skeletal related events like pain, pathologic fractures and paraparesis are common. These complications often occur during the last months of life; however, some patients will live for years. The aim of the study was to identify factors associated with survival.

Material and Methods: This retrospective study was based on a consecutive series of 100 patients with lung cancer treated surgically for metastatic lesions of long bones or due to vertebral fracture and paraparesis from 1986 through 2006. There were 45 men and 55 women with a median age of 60 and 63 years respectively. 68 patients were surgically treated for a long bone fracture and 32 patients due to paraparesis. Of the patients operated for a long bone fracture, 73 had a complete fracture whereas 33 were treated for an impending fracture. Adenocarcinoma was diagnosed in 60 patients, squamous cell carcinoma in 15, low differentiated non-small cell cancer in 11, SCLC in large cell carcinoma in 8, bronchoalveolar carcinoma 1 and large cell carcinoma in 5. 89% of male patients and 86% of the females were smokers or former smokers.

Results: The Kaplan-Meier survival rate for the series of 100 patients was 0.19 at 1 year after surgery, 0.07 at 2 years and 0.04 after 3 years. The median survival was 319 days for patients with adenocarcinoma, 253 days for patients with SCLC and 244 days for squamous cell carcinoma ($p<0.014$). 33% of the patients had skeletal metastasis as the first sign of disease. Their survival was significantly shorter than patients with bone metastasis diagnosed as a secondary event, 94 vs 319 days ($P<0.049$). Patients treated for a long bone fracture had a significantly longer survival than patients operated due to paraparesis 316 vs 207 days ($p<0.038$). There was a tendency to shorter survival in patients with complete as opposed to impending fractures ($p<0.07$).

Conclusion: The one year survival rate 0.19 implicates that palliative surgery is justified in patients with skeletal metastasis of lung cancer. However, patients with skeletal metastasis as the first sign of disease and patients surgically treated for paraparesis were associated with poor prognosis.

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The clinical experiences of double sleeve lobectomy of the bronchus and the pulmonary artery

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Objective: Investigate the methods and the results of double sleeve lobectomy of the bronchus and the pulmonary artery in surgical treatment for the central lung cancer.

Methods: From March 1995 to March 2006, double sleeve resection and reconstruction of bronchus and pulmonary artery was performed in 12 cases with central lung cancer. Among them, double sleeve left upper lobectomy in 10 cases, double sleeve right upper-middle lobectomy in 2 cases.

Results: Occurring irregular heartbeat after operation in 2 cases, the obstruction pneumonia and pulmonary atelectasis in 1 case. The squamous cell carcinoma in 9 cases, adenocarcinoma in 2 cases, SCLC in 1 case. No surgical operation death. The 1,3 and 5 year survival rate was 81.9% (9/11), 100%(7/7) and 100%(5/5) respectively.

Conclusion: The double sleeve lobectomy of bronchus and pulmonary artery maximally reserving the healthy lung and maximally cutting off the tumor at the same time, avoiding pneumonectomy. The postoperative living quality of patients is well.

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Tumor size and 5-year survival rate in surgically treated patients with pN0M0 NSCLC

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Background: In present TNM system the border line between T1 and T2 is 3cm of diameter in tumor size. We tried to estimate the influence of tumor size on the 5-year survival rate in MSCLC patients operated on with pN0M0.

Method: We have analyzed retrospectively the group of 328 patients with pN0 NSCLC operated on in our institution between year 1998 and 2000. The time of follow-up was 5 to 8 years.

We divided our pts into 7 groups considering the tumor size criteria (<1cm, 1-2cm, 2-3cm, 3-5cm, 5-7cm, 7- 0cm, > 10cm).

Results: The histology of resected tumors was adenocarcinoma in 108 (38%), squamous in 154 (47%), NSCLC in 10 (3.1%), large cell In 9 (2.7%), carcinoid in 22 (6.7%), other in 8 (2.4%). The type of resection included pneumonectomy in 56 pts, lobectomy in 263 pts and wedge resection/segmentectomy in 8 pts.

The number of pts incorporated in tumor size group was 10, 50 76, 100, 47 26 and 9 pts in 1cm group, 1-2cm group, 2-3cm group, 3-5cm group, 5-7cm group, 7-10cm and > 10cm group respectively. The 5-year survival rates were 80%, 78%, 79%, 57%, 59%, 44% and 33.3% respectively.

Conclusions: We have found no statistically significant deference between first three groups of patients. Therefore we concluded that the 5cm border line in tumor size might be prognostic in terms of 5-year survival rate in NSCLC patients undergoing radical resection of lung tissue.